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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte
GUNTHER BELLMANN, GUDRUN CLAUS-HERZ, and CHRISTOPH KESSLER

Appeal 2008-4551
Application 10/665,937
Technology Center 1600

Decided: October 10, 2008

Before DONALD E. ADAMS, LORA M. GREEN, and JEFFREY N. FREDMAN, *Administrative Patent Judges*.

FREDMAN, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims to an ophthalmic gel. We have jurisdiction under 35 U.S.C. § 6(b). We affirm.

Background

"Dexamethasone preparations are known in the form of eye-drops and eye ointments" (Spec. 1). The Specification notes that "[k]nown eye-drop formulations comprising dexamethasone esters as the active ingredient are adjusted to slightly alkaline pH values. For example, solutions of drops which are currently available commercially typically have a pH value of about 7.3" (Spec. 1).

Statement of the Case

The Claims

Claims 7-16 are on appeal. We will focus on claims 7 and 8, which are representative and reads as follows:

> 7. An ophthalmic gel preparation comprising:
> dexamethasone dihydrogenphosphate disodium;
> a gel forming, pharmaceutically acceptable substance in an amount effective for adjusting the viscosity of the preparation so that the preparation has the form of a gel; and
> a pH regulating component in an amount effective to provide the preparation with a pH value above 7.3.
>
> 8. The preparation according to claim 7, wherein the preparation has a pH value between 7.6 and 8.2.

The prior art

The Examiner relies on the following prior art references to show unpatentability:

Mazuel et al.	U.S. 4,861,760	Aug. 29, 1989
Rozier	U.S. 5,304,559	Apr. 19, 1994
Kamishita et al.	GB 2,007,091 A	May 16, 1979

The issue

The rejection as presented by the Examiner is as follows:

Claims 7-16 stand rejected under 35 U.S.C. § 103(a) as being obvious over Mazuel, Rozier, and Kamishita (Ans. 4).

35 U.S.C. § 103(a) rejection over Mazuel, Rozier, and Kamishita

Appellants argue that the "the cited references teach away from the presently claimed invention. In Example 3 of Mazuel et al., dexamethasone phosphate solutions are disclosed, but the solutions of Mazuel et al. are designed to gel only upon contact with the eye's liquid" (App. Br. 5). Appellants contend that "the present claims do not read on a formulation that gels upon exposure to eye fluid" (App. Br. 5-6).

Appellants further argue that none of the prior art references "recognizes any problem with stability of dexamethasone dihydrogenphosphate disodium-containing gel preparations; suggests adjusting pH to any value (let alone the pH value in the present claims) to solve the problem of storage stability for such preparations; nor discloses dexamethasone dihydrogenphosphate disodium-containing gel preparations with the claimed pH range" (App. Br. 7).

The Examiner responds that "The GB Patent teaches a gel formulation at the claimed PH [sic], which can contain dexamethasone derivatives. The other relied upon references teach the use of secondary components in such composition as old" (Ans. 5).

In view of these conflicting positions, we frame the obviousness issue before us as follows:

Would it have been obvious to an ordinary artisan to prepare the ophthalmic gel of claim 7 based on Mazuel, Rozier, and Kamishita?

Findings of Fact (FF)

1. Mazuel teaches "ophtalmic [sic] compositions . . . [which] are especially suitable for administering to the eye any pharmaceutically active substance administered for curative and/or diagnostic purposes" (Mazuel, col. 4, ll. 5-9).

2. Mazuel teaches "gel formation in a rabbit's eye following a 20 µl instillation of a solution containing 0.4% by weigh of Gelrite® deionized water" (Mazuel, col. 3, ll. 65-68).

3. Mazuel discloses the incorporation of dexamethasone sodium phosphate (Mazuel, col. 5, l. 61).

4. Mazuel teaches, in Example 3, an ophthalmic solution with 0.1% dexamethasone phosphate, 0.6% Gelrite®, 0.01% benzalkonium chloride, 4% mannitol and water (Mazuel, col. 7, ll. 50-65).

5. Mazuel teaches the use of "small amounts of acids or bases for adjusting the pH to values suitable for administration to the eye" (Mazuel, col. 4, ll. 47-49).

6. Rozier teaches that "the liquid/gel phase transition nature of the dispersant used enables the activity of the active principle contained in these compositions to be prolonged. In particular, in the treatment of ophthalmic disorders, this type of composition enables the drawbacks encountered with the standard formulations to be overcome" (Rozier, col. 2, ll. 8-15).

7. Rozier teaches "[p]referably, the pH of the composition according to the invention will be between about 8.0 and 8.5" (Rozier, col. 2, ll. 63-65).

8. Rozier teaches, in Example 2, an ophthalmic composition with Gelrite, mannitol and a norfloxacin active agent where the pH is between 8.0 and 8.5 (Rozier, col. 4, ll. 42-64).

9. Kamishita teaches "[a]n ophthalmic composition in the form of a gel comprises an aqueous solution of a carboxyvinyl polymer, a water-soluble basic substance and an ophthalmic drug admixed therewith, the gel having a pH of 5 to 8" (Kamishita, abstract).

10. Kamishita teaches "[e]xamples of ophthalmic drugs which can be used in the gel preparations of the present invention include . . . dexamethasone" (Kamishita, col. 2, ll. 116-120).

11. Kamishita teaches, in example 12, a dexamethasone ophthalmic gel with a pH of 7.05 (Kamishita, col. 4, ll. 5-14).

Discussion of the 35 U.S.C. § 103(a) rejection over Mazuel, Rozier, and Kamishita

Claim 7

We agree with the Examiner that it would have been prima facie obvious to one of skill in the art to combine the teachings of Mazuel, Rozier and Kamishita to arrive at an ophthalmic composition with a gel forming substance, dexamethasone sodium phosphate and a pH greater than 7.3. Mazuel teaches ophthalmic compositions which gels upon administration including a gel forming substance and dexamethasone sodium phosphate (FF 1-5). Rozier teaches an ophthalmic composition that gels upon

administration with a pH that is preferably between 8 and 8.5 (FF 6-8). Kamishita teaches an ophthalmic gel with dexamethazone in a pH range of 5 to 8 (FF 9-11).

In *KSR*, the Supreme Court stated that

> [t]he principles underlying these cases are instructive when the question is whether a patent claiming the combination of elements of prior art is obvious. When a work is available in one field of endeavor, design incentives and other market forces can prompt variations of it, either in the same field or a different one. If a person of ordinary skill can implement a predictable variation, §103 likely bars its patentability.

KSR Int'l v. Teleflex Inc., 127 S. Ct. 1727, 1740 (2007).

Applying the *KSR* standard of obviousness to the Examiner's findings and the findings of fact, we conclude that the combination of the ophthalmic gel with dexamethazone of Kamishita with a pH range of 5 to 8, the ophthalmic gel of Mazuel with dexamethasone sodium phosphate and the ophthalmic compositions of Rozier with preferred pH ranges of 8.0 to 8.5 represents a combination of known elements which yield the predictable use of modifying the ophthalmic composition of Kamishita to use dexamethasone sodium phosphate in the preferred pH ranges of 8 to 8.5 of Rozier. Such a combination is merely a "predictable use of prior art elements according to their established functions." *KSR*, 127 S. Ct. at 1740.

Appellants argue that the "claims do not read on a formulation that gels upon exposure to eye fluid" (App. Br. 5-6). We need not disagree with Appellants claim interpretation to disagree with Appellants conclusion regarding *prima facie* obviousness. While Appellants are correct that Mazuel's preparation does not gel until administration, Kamishita teaches an

ophthalmic composition in gel form (FF 9), which may include dexamethasone as a drug (FF 10).

We are not persuaded by Appellants' contention that the "rejection relies on selectively choosing various limitations of the present claims from the various cited references, without the requisite motivation" (App. Br. 6). In *KSR*, the Supreme Court rejected the rigid application of a "motivation" requirement. *See KSR*, 127 S. Ct. at 1741 ("The obviousness analysis cannot be confined by a formalistic conception of the words teaching, suggestion, and motivation."). We find that the Mazuel, Rozier and Kamishita demonstrate that an ophthalmic gel with dexamethasone sodium phosphate at a pH of 8 to 8.5 would have been a predictable variation based upon the findings of fact (FF 1-11).

Appellants then argue that they have "confirmed the stability data discussed in specification page 5, thereby rebutting any *prima facie* case of obviousness" (App. Br. 7).

However, we do not find this argument persuasive for several reasons. As a threshold reason, the stability data entered September 18, 2003 or in Appellants Appeal Brief was not properly submitted into the record. Appellants did not submit this evidence in the form of a Declaration, but simply attached some laboratory records to a preliminary amendment. According to 37 C.F.R. § 1.132, "any evidence submitted to traverse the rejection or objection on a basis not otherwise provided for must be by way of an oath or declaration under this section." Thus Applicants' stability data is without admissible evidentiary support and is not entitled to any weight. "[A]rguments of counsel cannot take the place of evidence lacking in the

record." *Estee Lauder Inc. v. L'Oreal, S.A.*, 129 F.3d 588, 595 (Fed. Cir. 1997) *quoting Knorr v. Pearson*, 671 F.2d 1368, 1373 (CCPA 1982). *See also, In re Lindner*, 457 F.2d 506, 508 (CCPA 1972) ("mere lawyers' arguments unsupported by factual evidence are insufficient").

Additionally, the discussion of the result in the Specification does not compare the formulation with the closest prior art of either Mazuel or Kamishita. *See In re Baxter-Travenol Labs.*, 952 F.2d 388, 392 (Fed. Cir. 1991) ("[W]hen unexpected results are used as evidence of nonobviousness, the results must be shown to be unexpected compared with the closest prior art.")

We also note that the comparison of Formulation 1 and Formulation C1, reproduced on page 8 of Appellants Brief, is not commensurate in scope with the claim, which encompasses any pH value greater than 7.3. "Commensurate in scope" means that the evidence provides a reasonable basis for concluding that the untested embodiments encompassed by the claims would behave in the same manner as the tested embodiment(s). *See Lindner*, 457 F.2d at 508 ("Here only one mixture of ingredients was tested. . . . The claims, however, are much broader in scope, . . . and we have to agree with the Patent Office that there is no 'adequate basis for reasonably concluding that the great number and variety of compositions included by the claims would behave in the same manner as the [single] tested composition.'") (bracketed material in original).

Additionally, the data shown in the Evidence appendix does not clearly identify which pH values were tested, or whether multiple values were tested (*see* App. Br. 18-20).

Claim 8

Appellants argue that the range of pH values listed in claim 8 is particularly not suggested by the prior art. However, Rozier does indicate that a pH of 8 to 8.5 is preferred (FF 7) and Kamishita suggests a pH range of 5 to 8 (FF 9). These ranges overlap the range of claim 8. "[A] prima facie case of obviousness arises when the ranges of a claimed composition overlap the ranges disclosed in the prior art." *In re Harris*, 409 F.3d 1339, 1341 (Fed. Cir. 2005).

As discussed above regarding claim 7, Appellants evidence was not properly filed and is not persuasive regarding unexpected results for the claimed range.

We affirm the rejection of claims 7 and 8 under 35 U.S.C. § 103(a) over Mazuel, Rozier, and Kamishita. Pursuant to 37 C.F.R. § 41.37(c)(1)(vii)(2006), we also affirm the rejections of claims 9-16 as these claims were not argued separately.

CONCLUSION

In summary, we affirm the rejection of claims 7 and 8 under 35 U.S.C. § 103(a) over Mazuel, Rozier, and Kamishita. Pursuant to 37 C.F.R. § 41.37(c)(1)(vii)(2006), we also affirm the rejections of claims 9-16 as these claims were not argued separately.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a)(1)(iv)(2006).

AFFIRMED

cdc

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